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EXAMINER	
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ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,432	ROE, CHARLES R.	
	Examiner	Art Unit	
	GREGG POLANSKY	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-17 and 21-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17 and 21-36* is/are rejected.

7)☒ Claim(s) *28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/19/2008 & 12/16/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's response, filed 10/29/2008, to the Office Action mailed 9/16/2008 is acknowledged. Applicant amended Claims 15, 17, and 23, and presented arguments in response to the Office Action.

2. Applicant's Information Disclosure Statements, filed 11/19/2008 and 12/16/2008, are acknowledged and have been reviewed.

3. Claims 15-17 and 21-36 are pending and presently under consideration.

4. Applicant's arguments have been fully considered and are persuasive in part. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Objections

5. Claim 28 is objected to because of the following informalities: Claim 28 has a period (".") between the words "provided" and "parenterally". MPEP 608.01(m) requires that each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck*, 36 USPQ2d 1211 (D.D.C. 1995). Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-17 and 21-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

The claims recite "seven carbon fatty acid selected from triheptanoin or n-heptanoic acid or derivatives thereof". There is insufficient written basis for derivatives of triheptanoin or n-heptanoic acid in the Specification.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plan for obtaining the claimed chemical invention." *Elli Liily*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by

"showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure..." *Enzo Biochem, Inc. v. Gen-Probe Inc.,* 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. At 1106 (emphasis added)). Moreover, although *Elli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

Applicant has failed to provide any structural characteristics, chemical formula, name(s) or physical properties of derivatives of triheptanoin or n-heptanoic acid, aside from the recitation in Claim 15 that such are contemplated. The Specification does not disclose any teaching of derivatives of triheptanoin or n-heptanoic acid .

Therefore, it is not apparent that Applicant was actually in possession of, and intended to use within the context of the present invention, any specific derivatives of triheptanoin or n-heptanoic acid at the time the present invention was made. The skilled artisan could not "immediately envisage" the claimed compounds based on the description in the disclosure.

Applicant argues that the Specification "provides numerous examples of the seven carbon fatty acid and derivatives thereof [and] the specification provides the structure and function of the claimed invention and numerous seven carbon fatty acid derivatives in paragraph [0076]". It is noted that paragraph [0076] of the Specification as originally filed does not disclose this information.

Applicant's arguments are not persuasive. The instant claims are drawn to "triheptanoin or n-heptanoic acid or derivatives thereof"; they are not drawn to derivatives of seven carbon fatty acids. Further, paragraph [0076] (at page 22 of the Specification) discloses the treatment of infants with fatty acid metabolism defects with triheptanoin. Derivatives of triheptanoin are not disclosed here or anywhere else in the Specification.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 15-17 and 21-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Odle et al. (Journal of Nutrition, 1991, Vol. 121, pages 605-614; provided by Applicant), in view of Ajinomoto (JP 52015834A (provided by Applicant)) and Jandacek et al. (US Patent No. 4,753,963).

Inhibition of mitochondrial β-oxidation of long-chain fatty acids, and its physiological effects, caused by a deficiency of acylcarnitine/carnitine translocase is well known by one of ordinary skill in the art, as is a test for acylcarnitine-carnitine translocase activity used in diagnosis of the deficiency (as evidenced by Kerner et al., "Genetic Disorders of Carnitine Metabolism and Their Nutritional Management", in Annual Review of Nutrition, 1998, Vol. 18, pages 179-206). See pages 192-193.

Odle et al. teach that changes in chain length within the medium-chain fatty acid family "may dramatically influence the rate and extent of digestion and/or absorption and metabolism of medium-chain triglycerides by neonates".

One of the benefits of the medium-chain fatty acids is their "preferential oxidation because of less dependence on carnitine acyltransferase/translocase system for entry into the mitochondria". See abstract and 1st paragraph, page 605. Odle et al. disclose studies of medium-chain triglycerides containing unsaturated 7, 8, 9, and 10 carbon fatty acids. The reference suggests propionyl-CoA arising from the β-oxidation of odd-carbon fatty acid triglycerides (7 carbon more pronounced than 9 carbon) could diminish the hyperketonemia associated with medium-chain triglycerides. See 1st 11 lines, left column, page 606; and the 1st half of the right column, page 612.

One of ordinary skill in the art would have found it obvious to utilize the teachings of Odle et al. to provide to individuals suffering from acylcarnitine/carnitine translocase deficiency more readily absorbed and metabolized fats (i.e., triglycerides of medium chain fatty acids, particularly 7 and 9 carbon-chain fatty acids, such as "tri-7:0", a triglyceride of heptanoic acid (triheptanoin)).

Ajinomoto teaches an oral (enteral) triheptanoin nutritional supplement that includes triheptanoin alone, or in combination with proteins, oils, carbohydrates, vitamins and minerals. The supplement can include a beverage, such as milk. The reference discloses the composition is readily absorbed from the digestive system to supply calories without participation of insulin (insulin sensitivity is frequently diminished

in premature infants) and without producing excess ketones (also taught by Odle et al., *supra*).

Triheptanoin is metabolized by the body to three molecules of heptanoic acid and glycerol. Therefore, administration of a composition comprising triheptanoin is equivalent to administration of a composition comprising heptanoic acid, as required by instant Claims 16 and 31. Indeed, the instant Specification (paragraph 70) discloses the "terms heptanoic acid, heptanoate, and triheptanoin may be used interchangeably".

The cited references do not teach specific dosages of triheptanoin.

Jandacek et al. discloses a nutritional fat suitable for enteral and parenteral products (see abstract). The fat disclosed by Jandacek et al. consists of triglycerides having the following formula:

wherein each R^1 group is selected from n-heptanoyl, n-octanoyl, n-nonanoyl, n-decanoyl and n-undecanoyl groups; and the R^2 groups comprise from 0 to about 90% saturated acyl groups selected from n-heptanoyl, n-octanoyl, n-nonanoyl, n-decanoyl, n-undecanoyl, lauroyl, myristoyl, palmitoyl, stearoyl and mixtures thereof; from 0 to about 90% oleoyl groups; from about 10 to 100% linoleoyl groups; and from 0 to about 10% linolenoyl groups.

When R1 and R2 are selected to be n-heptanoyl, this formula results in a nutritional fat compound that is identical to triheptanoin.

The reference is drawn to developing a nutritional fat in a form which is well absorbed by those persons such as infants which have fat malabsorption problems (column 1, lines 45-48). Jandacek et al. teaches enteral compositions comprising the nutritional fat (triglycerides) disclosed in the reference, a source of carbohydrates, a source of amino acids and optionally, components such as vitamins and minerals. The composition can be formulated as a dry mixture or mixed with water to provide a fluid formulation for enteral administration. See column 5, lines 1-9. The amount of the triglyceride utilized in the composition is a nutritionally effective amount, based upon the subject and the nutritional benefits required. The composition typically comprises the nutritional fat (triglyceride) in an amount of about 2% to about 20% by weight of the composition (about 18 to about 180 calories per 100 grams of composition or about 4% to about 36% of the total caloric value of the composition). See column 5, lines 18-20 and column 7, lines 5-8. The reference discloses oral and feeding tube administration of the composition. See column 4, last paragraph. Jandacek et al. also discloses parenterally administrable compositions. See column 6, lines 56-60).
As discussed *supra*, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the teachings of Odle et al., which suggest enhanced β-oxidation of odd-carbon fatty acid triglycerides (especially 7 carbon fatty acid triglycerides), to provide to individuals suffering from acylcarnitine/carnitine translocase deficiency (including in prematurely-born human infants) more readily absorbed and metabolized fats. The artisan would have been motivated to find suitable compositions taught in the art. Ajinomoto teaches such a composition (triheptanoin) and further

discloses its use as a suitable source of easily absorbed (fat derived) calories that do not require insulin for absorption (as would be required by a carbohydrate derived source of calories). These two references would have motivated the artisan to utilize the teachings of Jandacek et al., selecting a triglyceride comprised of 3 n-heptanoyl groups (i.e., triheptanoin). Jandacek et al. teaches compositions of triglycerides, disclosing concentration ranges for the triglycerides of said compositions (*supra*). It is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a claim are disclosed in the prior art. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955) and MPEP 2144.05(11). One of ordinary skill in the art would have adjusted triheptanoin concentrations and dosage schedules as appropriate, based upon factors such as, the age and weight of the patient, the severity of the condition being treated and the route of administration.

Applicant argues the reference to Odle et al do not teach treatment of humans having translocase deficiency and do not teach that a seven-carbon fatty acid is safe for human consumption or has any nutritional benefit to humans (much of the data presented by Odle et al. is from administration to neonatal pigs).

It would have been obvious to one of ordinary skill in the art to apply teachings of nutrition (e.g., dietary supplements, nutraceuticals and functional foods), derived from experiments with pigs, directly to humans. This is evidenced by the disclosure of the review article of Miller et al. ("The Pig as a Model for Human Nutrition", 1987, Annual Review of Nutrition, Vol. 7, pages 361-382). For example, Miller et al. teach pig and human nutrient requirements are similar in more ways than any other nonprimate

mammalian species, providing a basis for the use of the pig in many human nutritional studies. See page 363, 4th paragraph.

Applicant argues that while Ajinomoto may disclose a food having triheptanoin, "Ajinomoto states that the additives [(triheptanoin)] are **not necessarily pure e.g. may contain a small amount of fatty acids**"...[and] Ajinomoto fails to teach a composition stating that the food may have triheptanoin and that it is not necessarily pure" (emphasis by Applicant). Further, Applicant argues "Ajinomoto fails to enable anything as it fails to teach the used [sic] how to make and use the subject matter of that [which] is disclosed".

The argument that the triheptanoin taught by Ajinomoto is "not necessarily pure" is confusing since this is not required by the instant claims. Indeed, the instant claim language is open, allowing for the inclusion of additional elements. Additionally, the instant claims are not drawn to a method of making triheptanoin or any other agent or composition.

Applicant's argues the reference to Jandacek et al. does not anticipate the present invention because Jandacek et al. "does not enable one skilled in the art to practice the claimed invention, and does not place the allegedly disclosed matter in the possession of the public".

One cannot show nonobviousness by attacking references individually where the rejection is based on combinations of references. The reference to Jandacek et al. is part of a rejection under 35 U.S.C. 103(a) and is provided to demonstrate prior art

knowledge of fats (which can include triheptanoin) suitable for enteral and parenteral products.

Conclusion

9. Claims 15-17 and 21-36 are rejected.

10. No claims are allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614